Specific targeting of ovarian tumor-associated macrophages by large, anionic nanoparticles.

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Public Summary:
Current ovarian cancer treatment regimens can be aggressive, and push the outer limits of tolerability. This study demonstrates that negatively charged nanoparticles localize selectively at ovarian cancer metastases (not in healthy tissue) when they are administered into the abdomen. We show that the injected nanoparticles accumulate specifically in tumor-associated macrophages, making this targeted treatment approach especially profitable for existing immunotherapies targeting this cell population. This finding is exciting, because when the nanoparticles are pre-loaded with therapeutics, the off-target distribution of the drug should be drastically reduced. This would minimize the negative side-effects experienced by patients, and improve their quality of life while undergoing cancer treatment.

Scientific Abstract:
Immunotherapy is emerging as one of the most effective methods for treating many cancers. However, immunotherapy can still introduce significant off-target toxicity, and methods are sought to enable targeted immunotherapy at tumor sites. Here, we show that relatively large (>100-nm) anionic nanoparticles administered intraperitoneally (i.p.) selectively accumulate in tumor-associated macrophages (TAMs). In a mouse model of metastatic ovarian cancer, fluorescently labeled silica, poly(lactic-co-glycolic acid), and polystyrene nanoparticles administered i.p. were all found to selectively accumulate in TAMs. Quantifying silica particle uptake indicated that >80% of the injected dose was in TAMs. Particles that were smaller than 100 nm or cationic or administered intravenously (i.v.) showed no TAM targeting. Moreover, this phenomenon is likely to occur in humans because when freshly excised human surgical samples were treated with the fluorescent silica nanoparticles no interaction with healthy tissue was seen but selective uptake by TAMs was seen in 13 different patient samples. Ovarian cancer is a deadly disease that afflicts approximately 22,000 women per year in the United States, and the presence of immunosuppressive TAMs at tumors is correlated with decreased survival. The ability to selectively target TAMs opens the door to targeted immunotherapy for ovarian cancer.